

**TIME TO VIROLOGICAL SUPPRESSION AND SUBSEQUENT FAILURE  
IN ARV-NAÏVE SUBJECTS RECEIVING HAART: RESULTS FROM  
THE HIV-NAT 006 COHORT**



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A Thesis Submitted in Partial Fulfillment of the Requirements  
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A cohort study of virological suppression (to a plasma viral load [pVL] <50 copies), and subsequent virological failure (pVL rebounding to >50 copies), was conducted in antiretroviral therapy-naïve HIV patients in Thailand. Effects of time on highly active antiretroviral therapy (HAART) and of other characteristics on likelihood of suppression and failure were assessed with Kaplan-Meier product-limit curves, person-time logistic and Poisson regression, and Cox proportional hazards regression. Analysis included 404 subjects (221 males and 183 females), all of whom achieved suppression and 69 (17.1%) of whom experienced failure afterwards. The time intervals from starting HAART to suppression, and from suppression to failure or end of study, were examined.

Unstratified Kaplan-Meier curves exhibited two inflection points in the time courses of both suppression and failure (slow initial rise, then steep intermediate, then slow final rise). Thus, the time variable was modeled as the cubic polynomial of time on study in person-time regression models. Regressions were run with only the three terms for the time polynomial, yielding unadjusted time effect estimates. Bivariate analysis was conducted to evaluate effects of other independent variables separately on time to suppression and failure. Variables for which  $P < 0.2$  were entered into multivariable regression models, along with the 3 terms for the cubic polynomial of time, yielding adjusted time effect estimates.

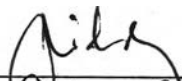
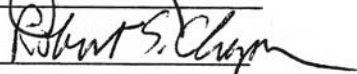
Unadjusted and adjusted time effects estimates were highly statistically significant for both suppression and failure ( $P < 0.001$ ). Furthermore, in both logistic and Poisson regressions, differences between unadjusted and adjusted time effects estimates were very small. These observations confirmed the appropriateness and robustness of modeling time with a cubic polynomial. There was no evidence that longer time was associated with increased likelihood of suppression or failure.

Final multivariable analysis identified a baseline regimen including a PI and a baseline pVL <50 000 as predictive of faster suppression (OR 1.87,  $P < 0.0001$ , OR 0.713,  $P = 0.005$  respectively) while a diagnosis of AIDS before baseline showed a trend to slower suppression (OR 0.87,  $P = 0.085$ ) Females were likely to fail more slowly (OR 0.57,  $P = 0.049$ ) while those with a baseline CD4 count >200 cells and those with a baseline pVL >50 000 copies were more likely to fail more quickly (OR 3.13,  $P < 0.0001$  and OR 1.94,  $P = 0.015$  respectively). A baseline regimen including a PI and suppressing before week 12 showed a trend to slower failure (OR 0.51,  $P = 0.089$  and OR 1.93,  $P = 0.058$  respectively). Covariate effects were similar in logistic, Poisson and Cox models.

Field of Study Health Systems Development Student's signature

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## TABLE OF CONTENTS

	Page
<b>ABSTRACT</b> .....	<b>iii</b>
<b>ACKNOWLEDGEMENTS</b> .....	<b>iv</b>
<b>TABLE OF CONTENTS</b> .....	<b>v</b>
<b>LIST OF TABLES</b> .....	<b>viii</b>
<b>LIST OF FIGURES</b> .....	<b>x</b>
<b>ACRONYMS AND ABBREVIATIONS</b> .....	<b>xii</b>
<b>CHAPTER I INTRODUCTION</b> .....	<b>1</b>
- The Situation in Thailand.....	1
- The Response in Thailand.....	3
- HAART .....	4
- HIV-NAT .....	5
- Why is this study needed?.....	6
- Research Questions .....	7
- Conceptual Framework .....	7
- Objectives.....	8
- Expected Outcomes.....	8
<b>CHAPTER II LITERATURE REVIEW</b> .....	<b>9</b>
- Search Methods .....	9
- Rates of Virological suppression .....	9
- Rates of Virological Failure .....	11
- Why is the length of time taking antiretroviral treatment important?.....	13
- Predictors of Virological Failure.....	15

	Page
- Summary .....	16
<b>CHAPTER III METHODS.....</b>	<b>17</b>
- Study Design and Scope.....	17
- The Viral Load Test .....	18
- Study Site .....	19
- Participants.....	19
- Sample Size.....	20
- Inclusion/Exclusion Criteria.....	22
- Data Collection, Processing and Analysis .....	22
- Time to Virological Suppression .....	24
- Time from Virological Suppression to Virological Failure .....	25
- Ethical Considerations .....	27
<b>CHAPTER IV RESULTS .....</b>	<b>28</b>
- The Study Population.....	28
- Baseline Characteristics .....	28
- Time to Virological Suppression .....	32
- Independent Variables (Covariates).....	35
- Results for Time from Start of HAART to Virological Suppression.....	35
- Modeling Time.....	36
- Bivariate Logistic Regression: from start of HAART to Virological Suppression .....	37
- Multiple Logistic Regression: Start of HAART to Virological Suppression...	39
- Time from Virological Suppression to Virological Failure .....	44

	Page
- Results for Time to Virological Failure .....	44
- Bivariate Logistic Regression: from Suppression to Virological Failure .....	46
- Multiple logistic regression: from Suppression to Virological Failure.....	48
<b>CHAPTER V DISCUSSIONS .....</b>	<b>57</b>
- Time Courses to Studied Events .....	58
- Time to Suppression.....	62
- Time to Virological Failure.....	67
- Limitations .....	70
<b>REFERENCES .....</b>	<b>73</b>
<b>APPENDICES.....</b>	<b>85</b>
APPENDIX A: Informed Consent Form for the HIVNAT 006 Study.....	86
APPENDIX B: Certificate of Ethics Approval HIVNAT 006 Study.....	88
APPENDIX C: Certificate of Ethical Approval for This Study.....	89
<b>CURRICULUM VITAE .....</b>	<b>94</b>

## LIST OF TABLES

Table	Page
1 Estimated Cumulative Numbers with HIV/AIDS in Thailand, 2004-2006.....	2
2 Global Summary of the AIDS Epidemic, December 2007 .....	2
3 Meta Analysis, Studies of Efficacy of AET Programs in Resource Poor Settings Showing Percentage with Undetectable PVL at Various Months (Mocroft et al., 2003) .....	12
4 Predictors of Virological Failure .....	15
5 Sample Size Calculations .....	21
6 Subject Characteristics .....	31
7 Medians and Interquartile Ranges .....	32
8 Results of Bivariate Logistic Regression from Start of HAART to Virological Suppression .....	38
9 Results of $\beta$ Estimates for time alone and with covariates in Multiple Logistic Regression .....	39
10 Results of Multiple Logistic Regressions from Start of HAART to Virological Suppression .....	40
11 Results of Bivariate Logistic Regression from Suppression to Virological Failure .....	47
12 Results of $\beta$ Estimates for time alone and with Covariates Selected for Multivariable Analysis.....	49
13 Results of Multiple Logistic Regressions for Time to Virological Failure Including Weight.....	50



Table	Page
14 Results of Multiple Logistic Regressions for Time to Virological Failure Without Weight .....	51
15 Comparison of Logistic and Poisson Regressions, Baseline to Virological Suppression for time .....	61
16 Comparison of Logistic, Poisson and Cox Regressions, Baseline to Virological Suppression for Covariates other than Time.....	61
17 Comparison of Logistic and Poisson Regressions, Suppression to Virological Failure for time.....	62
18 Comparison of Logistic and Poisson Regressions, Baseline to Virological Suppression for Covariates other than Time, Suppression to Virological Failure .....	63

## LIST OF FIGURES

Figure	Page
1 Conceptual framework .....	7
2 Proportion of Patients with Virological Failure by Region (Van Leth et al., 2004) Following 48 Weeks of HAART-error bars = 95% Confidence Intervals.....	13
3 Time to Virological Suppression.....	33
4 Distribution by Year of Entry onto Study .....	34
5 Kaplan-Meier Curve: Probability of Virological Suppression after Starting HAART.....	36
6 Kaplan-Meier Curve: Virological Suppression Stratified on Baseline Viral Load.....	41
7 Kaplan-Meier Curve: Virological Suppression Stratified on Baseline Regimen .....	41
8 Kaplan-Meier Curve: Virological Suppression Stratified on CDC Category ....	42
9 Overlay of Survival Curves with the Time Variable Unadjusted and Adjusted	42
10 Time to Virological Suppression Plotting Log Odds by Days of Follow-up .....	43
11 Distribution of the 69 Virological Failures.....	44
12 Kaplan-Meier Curve for Probability of Virological Failure.....	45
13 Kaplan-Meier Curve for Probability of Virological Failure Stratified on Gender .....	52
14 Kaplan-Meier Curve for Probability of Virological Failure Stratified on CD4+ Count at Baseline.....	52

Figure	Page
15 Kaplan-Meier Curve for Probability of Virological Failure Stratified on Plasma Viral Load.....	53
16 Kaplan-Meier Curve for Probability of Virological Failure Stratified on Baseline Regimen.....	54
17 Kaplan-Meier Curve for Probability of Virological Failure Stratified on Time to Virological Suppression .....	54
18 Overlay of Survival Curves for Virological Failure with the time Variable Unadjusted and Adjusted .....	55
19 Time from Virological Suppression to Virological Failure Plotting Log Odds by Days of Follow-up.....	56

## ACRONYMS AND ABBREVIATIONS

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
CDC	Centers for Disease Control
DOB	Date of birth
FDA	Food and Drug Administration
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
HIV-NAT	The HIV Netherlands, Australia, Thailand Research Collaboration
HIV-RNA	Human immunodeficiency virus ribonucleic acid
IATEC	International Antiviral Therapy Evaluation Centre (Amsterdam)
IDU	Intravenous drug user
MOPH	Ministry of Public Health
NAPHA	National Access to Antiretroviral Programs for HIV/AIDS (Thailand)
NCHECR	National Centre for HIV Epidemiology and Clinical Research (Sydney)
NNRTI	Non-nucleoside reverse transcriptase inhibitors
NRTI	Nucleoside reverse transcriptase inhibitor
PI	Protease inhibitor
PLWHA	People living with HIV/AIDS
pVL	Plasma viral load
SQV	Saquinavir
TRCARC	The Thai Red Cross AIDS Research Centre